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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/277,575	03/27/1999	MARTHA KAREN NEWELL	V00139/70028	3748
7590 12/19/2003 HELEN C LOCKHART WOLF GREENFIELD & SACKS 600 ATLANTIC AVENUE BOSTON, MA 02210			EXAMINER VANDERVEGT, FRANCOIS P	
			ART UNIT 1644	PAPER NUMBER

DATE MAILED: 12/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/277,575

Applicant(s)

NEWELL, MARTHA KAREN

Examiner

F. Pierre VanderVegt

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 August 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14, 18, 29, 39, 44, 47, 49, 74, 79, 140, 143, 144, 147 and 148 is/are pending in the application.
- 4a) Of the above claim(s) 5, 6, 14, 18, 29, 47, 49-53, 74, 79 and 140 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4, 7-13, 39, 44, 143, 144, 147 and 148 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

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### DETAILED ACTION

The Examiner in charge of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to F. Pierre VanderVegt, Ph.D. in Art Unit 1644.

This application claims the benefit of the filing date of provisional applications 60/082,250, 60/101,580 and 60/094,519.

Claims 15-17, 19-28, 30-38, 40-43, 45-46, 48, 54-73, 75-78, 80-139, 141-142, 145 and 146 have been canceled.

Claims 1-14, 18, 29, 39, 44, 47, 49, 74, 79, 140, 143, 144, 147 and 148 are currently pending.

Claims 5-6, 14, 18, 29, 47, 49-53, 74, 79, and 140 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention

Claims 1-4, 7-13, 39, 44, 143-144, and 147-148 are the subject of examination in the present Office Action.

In view of Applicant's amendment and remarks and the declaration under 37 CFR § 1.132 of Martha Karen Newell filed August 25, 2003 only the following ground of rejection is maintained.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-4, 7-13, 39, 44, 143-144 and 147-148 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for decreasing mitochondrial membrane potential in a mammalian cell and for inducing the expression of the immune molecule of MHC Class II HLA-DR, comprising administering an MHC class II ligand, does not reasonably provide enablement for said method wherein said method comprises the additional step of contacting said cell with an amount of an MHC Class II HLA-DR inducing agent effective to induce expression of any immune molecule including MHC class II HLA-DR on the surface of the mammalian cell, wherein said agent is any fatty acid. The specification does not enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

It was previously stated: "The instant claims are drawn to a method for decreasing mitochondrial membrane potential in a mammalian cell comprising administering an MHC class II ligand, and a method for decreasing mitochondrial membrane potential in a mammalian cell comprising administering an MHC class II ligand wherein said method comprises the additional step of contacting said cell with an amount of of an MHC Class II HLA-DR inducing agent effective to induce expression of MHC class II HLA-DR on the surface of the mammalian cell, wherein said agent is a fatty acid.

The instant specification discloses on page 7 that a fatty acid is a preferred MHC Class II HLA-DR inducing agent which induces expression of MHC Class II on the cell surface. And the specification discloses on page 96 that Figure 22 shows that in an in vitro assay in which the fatty acid oleic acid was used a carbon source, the leukemic tumor cell line L1210 used oleic acid at a much lower rate than the methotrexate resistant derivative leukemic cell line L1210DDP. However the instant specification does not exemplify that oleic acid or any other fatty acid, induces HLA-DR expression. A search of the art at the time the invention was made does not appear to teach that fatty acid induces HLA-DR expression. Therefore, in view of the state of the art at the time the invention was made regarding the ability of a fatty acid to induce HLA-DR expression, and given the insufficient guidance in the specification regarding the ability of a fatty acid to induce the expression of HLA-DR, it would require undue experimentation for one of skill to practice the claimed method which encompasses inducing HLA-DR expression with a fatty acid, without further direction from the specification."

Applicant's arguments and the declaration of Martha Karen Newell filed August 25, 2003 have been fully considered but are not persuasive.

The Newell declaration discloses experiments intended to show that treatment of a tumor cell with a fatty acid can induce expression of MHC class II on the surface of the tumor cells. The experiments show the growth of the low lipid cell line 60-7/LL on a low lipid growth medium. The experiment show that incubation of the cells with oleoyl S-CoA induces the expression of HLA-DR on the cells. The declaration is insufficient to overcome the ground of rejection for several reasons. First, the identity of what type of cell 60-7/LL is is not disclosed. Is 60-7/LL an antigen presenting cell, which normally would express MHC class II, or is the cell type from which 60-7/LL is derived normally a non-MHC class II-expressing cell type? Second, in vitro stimulation of a low-lipid cell type on a low-lipid medium with lipid is not believed to be an adequate demonstration of in vivo or ex vivo conditions that the claimed invention reads upon. Standard media and the in vivo milieu are not lipid deprived environments. Accordingly, it is not supported by the data shown that addition of fatty acids to either the ex vivo or in vivo environments would have any effect upon a population of tumor cells. Third, the experiment utilized a homogeneous population of cells. There is no evidence that such an administration of fatty acid can be adequately targeted to a particular type of cell, such as a tumor cell, in the in vivo environment. Fourth, the cells were treated with a preparation comprising the fatty acid oleoyl and the cofactor CoA (coenzyme A). it is not clear from the data presented as to whether the effect on MHC class

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II expression was caused by the fatty acid or the cofactor. Accordingly, the declaration of Dr. Newell is not persuasive and the ground of rejection stands. Claims not reciting "fatty acid" are included in the ground of rejection because they also read upon the use thereof.

**The following represents a new ground of rejection not necessitated by Applicant's amendment. Accordingly, this Office Action is made NON-FINAL.**

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 2, 13, 39, 143 and 144 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The burden of the written description requirement in this application for decreasing mitochondrial membrane potential in tumor cells by administering an MHC class II ligand to the cell to engage MHC class II on the surface of the cell in its broadest sense has not been met.

The written description in this case only sets forth tumor cells that express HLA-DR if those cells have been treated with "an MHC class II HLA-DR inducing agent." It is well known in the art that MHC class II antigens are selectively expressed on antigen presenting cells, however not all tumor cells are antigen presenting cells.

*Vas-Cath Inc. v. Mahurkar* ((CAFC, 1991) 19 USPQ2d 1111), clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See *Vas-Cath* at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see *Vas-Cath* at page 1115).

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With the exception of tumor cells that express HLA-DR as the result of treatment with an MHC class II HLA-DR inducing agent the skilled artisan cannot envision the encompassed tumor cells. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, ((CAFC, 1993) 25 USPQ 2d 1601) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, ((CAFC, 1991) 18 USPQ2d 1016).

Therefore only transport of biologically active compounds into a cell using the monoclonal anti-DNA antibody 3E10, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claim 44 is rejected under 35 U.S.C. 102(b) as being anticipated by Burrows et al. Cancer Research 52:2954 Abstract (of record).

Burrows teaches a murine model in which anti-MHC Class II antibody is administered in mice that were administered neuroblastoma transfected with the interferon gamma gene. Burrows et al teaches MHC was induced on the tumor vasculature endothelium, B lymphocytes, macrophages and some epithelial cells. The limitation of decreasing the membrane potential of the cell would be an inherent property resulting from the administration of the anti-MHC Class II antibody. Therefore, the referenced teachings anticipate the claimed invention.

Applicant contends that the Burrows reference does not anticipate the claimed invention because Burrows does not teach the induction of MHC class II expression on tumor cells. However, the present claim is not specifically drawn to tumor cells. Accordingly, the vasculature cells taught by Burrows satisfy the metes and bounds of the claim.

### ***Conclusion***

3. No claim is allowed.

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4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (703) 305-4441. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

**As of January 7, 2004, the Examiner's telephone number will be (571) 272-0852.**

F. Pierre VanderVegt, Ph.D. *RV*  
Patent Examiner  
December 12, 2003

*Patrick J. Nolan*  
PATRICK J. NOLAN, PH.D.  
PRIMARY EXAMINER

*12/12/03*